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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/357,349	07/14/99	GEERTS	H 36813.3

HM12/1004

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EXAMINER	
TURNER, S	
ART UNIT	**PAPER NUMBER**
1647	20

DATE MAILED: 10/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/357,349	Geerts et al.
Examiner	**Art Unit**
Sharon L. Turner, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 7-19-01 .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 7-9, 17, 18, 24, 41, 44, 58, and 59 is/are pending in the application.

4a) Of the above, claim(s) 17, 18, 24, 41, 44, 58, and 59 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 7-9 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims 7-9, 17, 18, 24, 41, 44, 58, and 59 are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☒ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 8

18) ☒ Interview Summary (PTO-413) Paper No(s). 20 (21)

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Priority

1. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the United Kingdom on 7-14-98. It is noted, however, that applicant has not filed a certified copy of the 9815283.8 application as required by 35 U.S.C. 119(b). Prior art is applied accordingly.

Election/Restriction

3. Claims 7-9, 17-18, 24, 41, 44 and 58-59 are pending.

4. Applicant's election of Group I, claims 7-9 (SEQ ID NO:3) in Paper No. 19 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5. Claims 17-18, 24, 41, 44 and 58-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 19.

Sequence Requirements

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

In particular it is noted that applicant has not amended the description of the drawings at p. 25-26 and 29-31 in reference to Figures 1-3, 21 and 23-24 so as to refer to all represented sequences by SEQ ID NO.

Specification

7. It is suggested that applicant incorporate the subject heading "Brief Description of the Drawings" to the section preceding the brief description of the drawings at p. 25.

Claim Objections

8. Claim 7 is objected to because of the following informalities: It is suggested that a comma be inserted between "encoding said growth factor or a functional equivalent," such that it

is clear that the "or" is modifying the growth factor and not the nucleic acid. Appropriate correction is required.

9. Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 9 does not appear to further limit claim 7 from which it depends as it contains the same structural features as recited in claim 7.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 7-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification discloses SEQ ID NO's: 3 and 4 which correspond to human enovin polypeptide. These SEQ ID NO's meet the written description provisions of 35 USC 112, first paragraph. However, the claims are directed to or encompass corresponding sequences from other species, mutated sequences, allelic variants, splice variants, and sequences that have a recited degree of identity, similarity or homology as encompassed by the claimed recitation of

"functional equivalents, derivatives or bioprecursors of said growth factor." None of these alternative sequences meets the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is for purposes of the 'written description' inquiry, whatever is now claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO's:3 and 4 of the instant application, the skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic and amino acid sequences and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The specific nucleic and amino acids are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO's:3 and 4 , but not the full breadth of claims meet the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath

makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

12. Claim rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the neurite outgrowth promoting effects and abrogation of taxol induced sensory deficits by disclosed enovin of SEQ ID NO:3 and 4, does not reasonably provide enablement for functional equivalents, derivatives or bioprecursors of said growth factor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

Instant specification discloses human enovin peptide sequences (SEQ ID Nos: 3 and 4). Instant specification also contemplates functional equivalents, derivatives and bioprecursors of these disclosed sequences. Yet, the specification fails to disclose any such sequences which correspond to such recitations or which retain enovin's disclosed functional activity.

Nevertheless applicants claims are directed to such functional equivalents, derivatives and bioprecursors thereof.

The specification does not enable this broad scope of the claims which encompasses alternative molecules because the specification does not teach which residues can or should be modified such that the polypeptides retain sufficient structural similarity to effect enovin function. The specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful and the skilled artisan at the time of the invention would not expect functional conservation among homologous sequences. Thus, applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims.

The skilled artisan readily recognizes that even today protein chemistry is an unpredictable area of biotechnology. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39, 2000. For example, Jobling et al, Mol. Microbiol., 1991, 5(7):1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which produce proteins that differ in native conformation, immunological recognition, binding and toxicity. Thus, Jobling exemplifies the importance of conserved structure to biological function. In view of the lack of guidance, the skilled artisan would be forced into undue experimentation in order to determine those peptides which correlate to the recitations of the claims, i.e., to define which residues are responsible for enovin function. Further the artisan would be forced to confirm the variant peptide's utility for neurite outgrowth and abrogation of taxol induced sensory deficits.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable, and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

Thus, for the aforementioned reasons one of skill in the art could not make or use the claimed invention without further undue experimentation.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 7-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "functional equivalents, derivatives and bioprecursors" of the said growth factors. However, the specification fails to define the structural or functional meets and bounds of the claim such that the skilled artisan can readily discern those molecules encompassed or excluded from the claim. Therefore, the limitations "functional equivalents, derivatives and bioprecursors" are indefinite to the skilled artisan.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

16. Claims 7-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Baloh et al., Neuron, 21:1291-1302, Dec. 1998.

Baloh et al., correspond with 100% similarity to SEQ ID NO:3 and 4 of instant claims. Thus, all characteristics of the claimed invention are necessarily and inherently provided by the Baloh peptide. In addition, Baloh teaches that their peptide, Artemin, is capable of supporting peripheral and central neurons, including extension and signals through the GFR alpha 3-RET receptor complex. Thus, the reference teachings anticipate the claimed invention.

17. Claims 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al., Science, 260:1130-1302, May 1993.

Lin et al., teach human GDNF precursor which shares 28% similarity with instant SEQ ID NO:3 and 4 and is a functional equivalent as the peptide enhances the survival, neurite outgrowth and differentiation of dopaminergic neurons, see in particular, Abstract. Thus, the reference teachings anticipate the claimed invention.

18. Claims 7-9 are rejected under 35 U.S.C. 102(e) as being anticipated by Johnson et al., US Patent 5,747,655 filed Nov. 1, 1996 and issued May 5, 1998.

Johnson et al., teach neurturin peptide which shares 38.6% sequence similarity with instant SEQ ID NOs:3 and 4 and thus is a functional equivalent and bioprecursor of instantly claimed enovin of SEQ ID NOs:3 and 4. The peptide is a neuronal growth factor which supports the survival and outgrowth (neurite extension) of superior cervical ganglion neurons, see in particular Figures 3 and 4. Thus, the reference teachings anticipate the claimed invention.

Status of Claims

19. No claims are allowed.

20. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
September 27, 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud